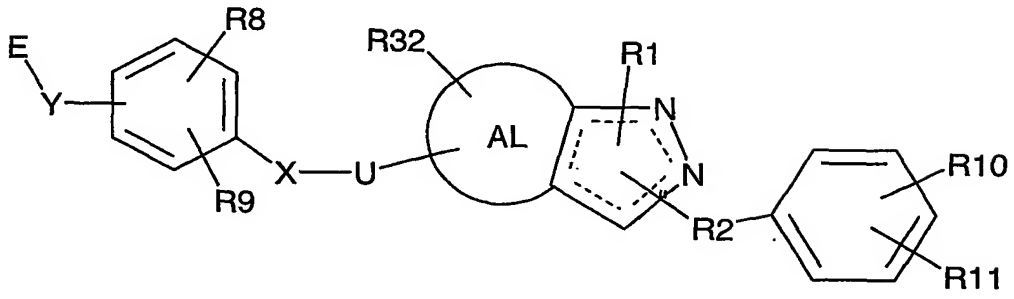
CLAIMS

What is claimed is:

1. A compound of the structural Formula I:



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R1 is selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and, wherein C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

(b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryloxy, aryl-C_{0-4}-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, $OS(O)_2R16$, $N(R17)_2$, NR18C(O)R19, $NR20SO_2R21$, SR22, S(O)R23, $S(O)_2R24$, and $S(O)_2N(R25)_2$; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

(c) R2 is selected from the group consisting of C_0-C_8 alkyl and C_{1-4}-heteroalkyl;

(d) X is selected from the group consisting of a single bond, O, S, $S(O)_2$ and N;

(e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;

(f) Y is selected from the group consisting of C, NH, and a single bond;

(g) E is C(R3)(R4)A or A and wherein

(i) A is selected from the group consisting of carboxyl, tetrazole, C_1-C_6 alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R^7;

(ii) each R^7 is independently selected from the group consisting of hydrogen, C_1-C_6 haloalkyl, aryl C_0-C_4 alkyl and C_1-C_6 alkyl;

(iii) R3 is selected from the group consisting of hydrogen, C_1-C_5 alkyl, and C_1-C_5 alkoxy; and

(iv) R4 is selected from the group consisting of H, C_1-C_5 alkyl, C_1-C_5 alkoxy, aryloxy, C_3-C_6 cycloalkyl, and aryl C_0-C_4 alkyl, and R3 and R4 are optionally combined to form a C_3-C_4 cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

(h) R8 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, and halo;

(i) R9 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, halo, aryl-C_0-C_4 alkyl, heteroaryl, C_1-C_6 allyl, SR29, and OR29, and wherein aryl-C_0-C_4 alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C_1-C_4 alkylenyl, and C_1-C_4 alkyl; R8 and R9 optionally combine to form a five membered fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;

(j) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12'', C_0-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', $OS(O)_2R16'$, $N(R17')_2$, NR18'C(O)R19', NR20'SO_2R21', SR22', S(O)R23', $S(O)_2R24'$, and $S(O)_2N(R25')_2$; and wherein aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(k) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

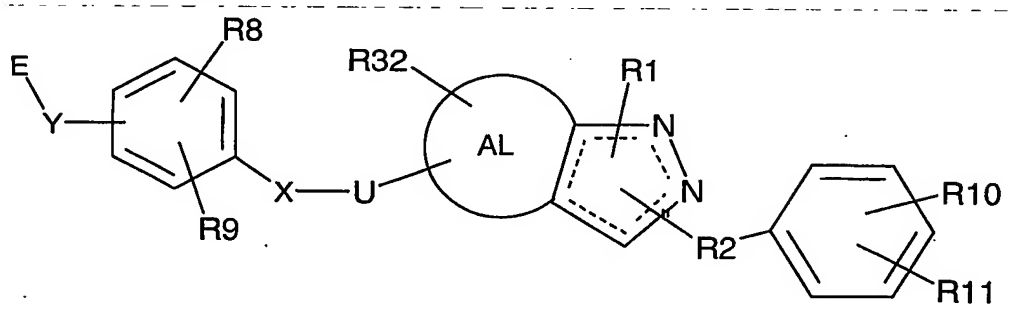
(l) R30 is selected from the group consisting of C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and wherein C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(m) R32 is selected from the group consisting of a bond, hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 alkyloxo;

(n) AL is selected from the group consisting of a fused C_3-C_8 carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and

(o) ---- is each optionally a bond to form a double bond at the indicated position.

2. A compound of the structural Formula II:



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R1 is selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and, wherein C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C_3-C_6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

(b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryloxy, aryl-C_{0-4}-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, $OS(O)_2R16$, $N(R17)_2$, NR18C(O)R19, $NR20SO_2R21$, SR22, S(O)R23, $S(O)_2R24$, and $S(O)_2N(R25)_2$; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

(c) R2 is selected from the group consisting of C_0-C_8 alkyl and C_{1-4}-heteroalkyl;

(d) X is selected from the group consisting of a single bond, O, S, $S(O)_2$ and N;

(e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is substituted with from one to four substituents each independently selected from R30;

(f) Y is selected from the group consisting of C, O, S, NH and a single bond;

(g) E is C(R3)(R4)A or A and wherein

(i) A is selected from the group consisting of carboxyl, tetrazole, C_1-C_6 alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R^7;

(ii) each R^7 is independently selected from the group consisting of hydrogen, C_1-C_6 haloalkyl, aryl C_0-C_4 alkyl and C_1-C_6 alkyl;

(iii) R3 is selected from the group consisting of hydrogen, C_1-C_5 alkyl, and C_1-C_5 alkoxy; and

(iv) R4 is selected from the group consisting of H, C_1-C_5 alkyl, C_1-C_5 alkoxy, aryloxy, C_3-C_6 cycloalkyl, and aryl C_0-C_4 alkyl, and R3 and R4 are optionally combined to form a C_3-C_4 cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

(h) R8 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, and halo;

(i) R9 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, halo, aryl-C_0-C_4 alkyl, heteroaryl, C_1-C_6 allyl, SR29, and OR29, and wherein aryl-C_0-C_4 alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C_1-C_4 alkylenyl, and C_1-C_4 alkyl; R8 and R9 optionally combine to form a five membered fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;

(j) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12'', C_0-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', $OS(O)_2R16'$, $N(R17')_2$, NR18'C(O)R19', $NR20'SO_2R21'$, SR22', S(O)R23', $S(O)_2R24'$, and $S(O)_2N(R25')_2$; and wherein aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(k) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

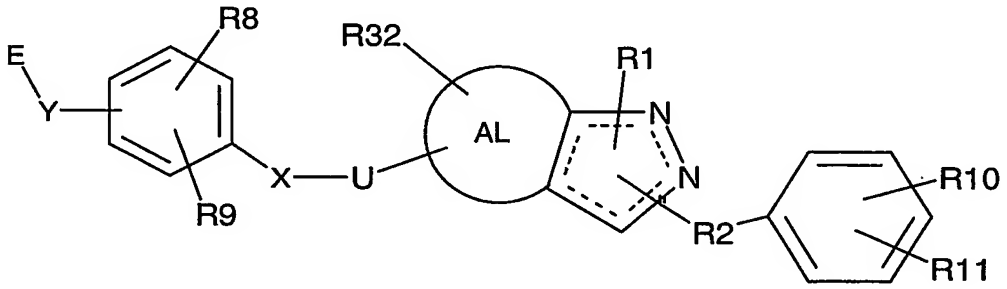
(l) R30 is selected from the group consisting of C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C_3-C_6 cycloalkylaryl-C_{0-2}-alkyl, and wherein C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C_3-C_6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(m)R32 is selected from the group consisting of a bond, hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 alkyloxo;

(n) AL is selected from the group consisting of a fused C_3-C_8 carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and

(o) ---- is each optionally a bond to form a double bond at the indicated position.

3. A compound of the structural Formula III:



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

(a) R1 is selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C3-C6 cycloalkylaryl-C_{0-2}-alkyl, and, wherein C_1-C_8 alkyl, C_1-C_8 alkenyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C_3-C_6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

(b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryloxy, aryl-C_{0-4}-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15,

$OS(O)_2R16$, $N(R17)_2$, $NR18C(O)R19$, $NR20SO_2R21$, $SR22$, $S(O)R23$, $S(O)_2R24$, and $S(O)_2N(R25)_2$; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

(c) R2 is selected from the group consisting of C_0-C_8 alkyl and C_{1-4}-heteroalkyl;

(d) X is selected from the group consisting of a single bond, O, S, $S(O)_2$ and N;

(e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;

(f) Y is selected from the group consisting of C, O, S, NH and a single bond;

(g) E is C(R3)(R4)A or A and wherein

(i) A is selected from the group consisting of carboxyl, tetrazole, C_1-C_6 alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R^7;

(ii) each R^7 is independently selected from the group consisting of hydrogen, C_1-C_6 haloalkyl, aryl C_0-C_4 alkyl and C_1-C_6 alkyl;

(iii) R3 is selected from the group consisting of hydrogen, C_1-C_5 alkyl, and C_1-C_5 alkoxy; and

(iv) R4 is selected from the group consisting of H, C_1-C_5 alkyl, C_1-C_5 alkoxy, aryloxy, C_3-C_6 cycloalkyl, and aryl C_0-C_4 alkyl, and R3 and R4 are optionally combined to form a C_3-C_4 cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

with the proviso that when Y is O then R4 is selected from the group consisting of C_1-C_5 alkyl, C_1-C_5 alkoxy, aryloxy, C_3-C_6 cycloalkyl, and aryl C_0-C_4 alkyl, and R3 and R4 are optionally combined to form a C_3-C_4 cycloalkyl, and wherein alkyl, alkoxy, cycloalkyl and aryl-

alkyl are each optionally substituted with one to three each independently selected from R26;

(h) R8 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, and halo;

(i) R9 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylenyl, halo, aryl-C_0-C_4 alkyl, heteroaryl, C_1-C_6 allyl, SR29, and OR29, and wherein aryl-C_0-C_4 alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C_1-C_4 alkylenyl, and C_1-C_4 alkyl; R8 and R9 optionally combine to form a five membered fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;

(j) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12'', C_0-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkyloxy, C_3-C_7 cycloalkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C_3-C_6 cycloalkylaryl-C_{0-2}-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', $OS(O)_2R16'$, $N(R17')_2$, NR18'C(O)R19', NR20'SO_2R21', SR22', S(O)R23', $S(O)_2R24'$, and $S(O)_2N(R25')_2$; and wherein aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(k) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl;

(l) R30 is selected from the group consisting of C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C_3-C_6 cycloalkylaryl-C_{0-2}-alkyl, and wherein C_1-C_6 alkyl, aryl-C_{0-4}-alkyl, aryl- C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, and C3-C6 cycloalkylaryl-C_{0-2}-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(m)R32 is selected from the group consisting of a bond, hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 alkyloxo;

(n) AL is selected from the group consisting of a fused C_3-C_8 carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and

(o) ---- is each optionally a bond to form a double bond at the indicated position.

4. A compound as claimed by Claim 1 wherein X is -O-.

5. A compound as claimed by Claim 1 wherein X is -S-.

6. A compound as claimed by any one of Claims 1 through 5 wherein Y is O.

7. A compound as claimed by any one of Claims 1 through 5 wherein Y is C.

8. A compound as claimed by any one of Claims 1 through 5 wherein wherein Y is S.

9. A compound as claimed by any one of Claims 1 through 8 wherein AL is a fused phenyl.

10. A compound as claimed by any one of Claims 1 through 8 wherein AL is a fused cycloalkyl.

11. A compound as claimed by any one of Claims 1 through 8 wherein AL is a fused pyrimidinyl.

12. A compound as claimed by any one of Claims 1 through 8 wherein AL is a fused pyridinyl.

13. A compound as claimed by any one of Claims 1 through 8 or Claim 15 wherein ---- is a bond to form a double bond at the designated location on Formula I.

14. A compound as claimed by any one of Claims 1 through 13 wherein E is C(R3)(R4)A.

15. A compound as claimed by any one of Claims 1 through 13 wherein E is A.

16. A compound as claimed by any one of Claims 1 through 14 wherein A is COOH.

17. A compound as claimed by any one of Claims 1 through 16 wherein R10 is haloalkyl.

18. A compound as claimed by any one of Claims 1 through 17 wherein R10 is CF_3.

19. A compound as claimed by any one of Claims 1 through 16 wherein R10 is haloalkyloxy.

20. A compound as claimed by any one of Claims 1 through 16 wherein R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-COOR12'', C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_1-C_6 haloalkyloxy.

21. A compound as claimed by any one of Claims 1 through 16 wherein R10 is selected from the group consisting of C_3-C_7 cycloalkyl, aryl-C_{0-4}-alkyl, aryl-C_{1-4}-heteroalkyl, heteroaryl-C_{0-4}-alkyl, C_3-C_6 cycloalkylaryl-C_{0-2}-alkyl, and aryloxy.

22. A compound as claimed by any one of Claims 1 through 21 wherein R8 is selected from the group consisting of C_1-C_3 alkyl and C_1-C_4 alkylenyl.

23. A compound as claimed by any one of Claims 1 through 21, wherein R8 and R9 are each independently selected from the group consisting of hydrogen and C_1-C_3 alkyl.

24. A compound as claimed by any one of Claims 1 through 22 wherein R29 is C_1-C_4 alkylenyl.

25. A compound as claimed by any one of Claims 1 through 22 and 24 wherein R8 is C_1-C_4 alkylenyl.

26. A compound as claimed by any one of Claims 1 through 22, 24, and 25 wherein R9 is OR29.

27. A compound as claimed by any one of Claims 1 through 22, 24, and 25 wherein R9 is SR29.

28. A compound as claimed by any one of Claims 1 through 22, 24 through 25 wherein R8 and R9 combine to form a fused bicyclic.

29. A compound as claimed by any one of Claims 1 through 28 wherein R1, R2, R3, and R4 are each independently selected from the group consisting of C_1-C_2 alkyl.

30. A compound as claimed by any one of Claims 1 through 28 wherein R1, R3, and R4 are each independently selected from the group consisting of hydrogen and C_1-C_2 alkyl.

31. A compound as claimed by any one of Claims 1 through 28 and 30 wherein R2 is a bond.

32. A compound as claimed by any one of Claims 1 through 31 wherein U is C_1-C_3 alkyl.

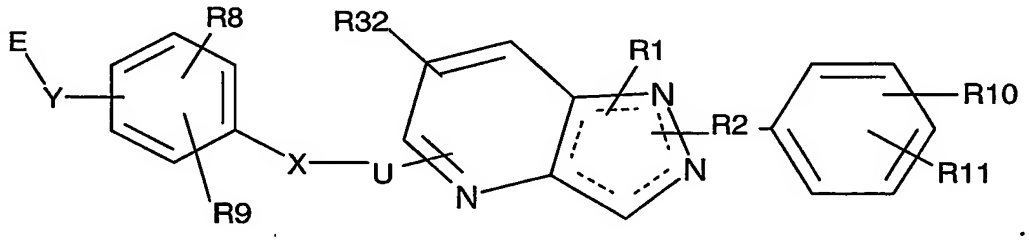
33. A compound as claimed by Claim 32 wherein U is saturated.

34. A compound as claimed by any one of Claims 32 or 33 wherein U is substituted with C_1-C_3 alkyl.

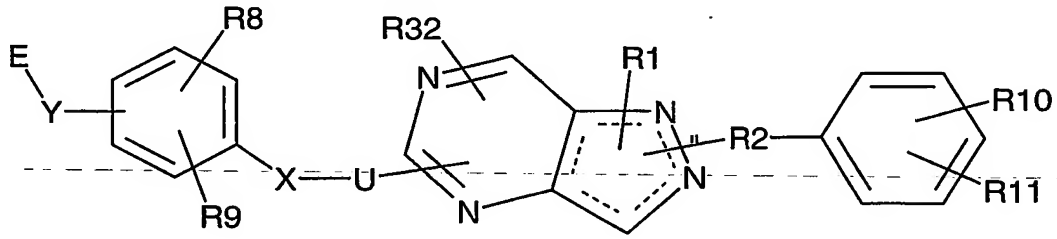
35. A compound as claimed by any one of Claims 1 through 34 wherein aliphatic linker is substituted with from one to four substituents each independently selected from the group consisting of R30.

36. A compound as claimed by any one of Claims 1 through 33, 34, and 35 wherein one carbon of the aliphatic linker is replaced with an –O-.

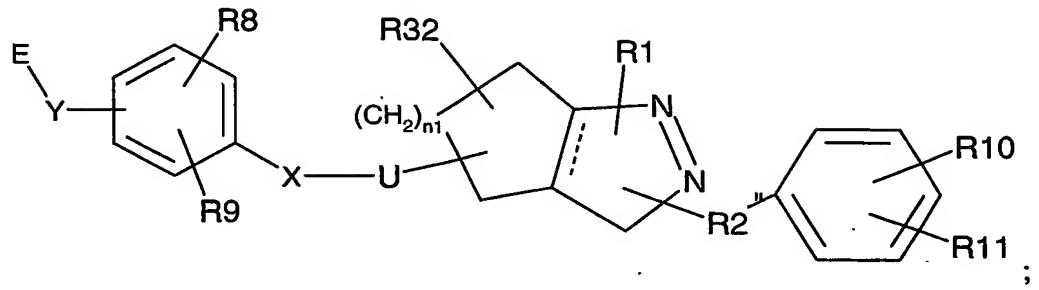
37. A compound as claimed by any one of Claims 1 through 4, 7, 8, 9, Claims 13 through 27, Claims 29 through 36 of the Structural Formula:



38. A compound as claimed by any one of Claims 1 through 5, 8, 9, Claims 12 through 27 Claims 29 through 36 of the Structural Formula:



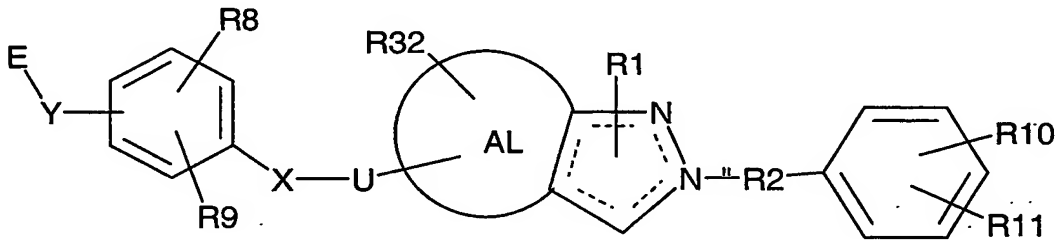
39. A compound as claimed by any one of Claims 1 through 11, 15, Claims 18 through 32, Claims 34 through 36 of the Structural Formula IV:



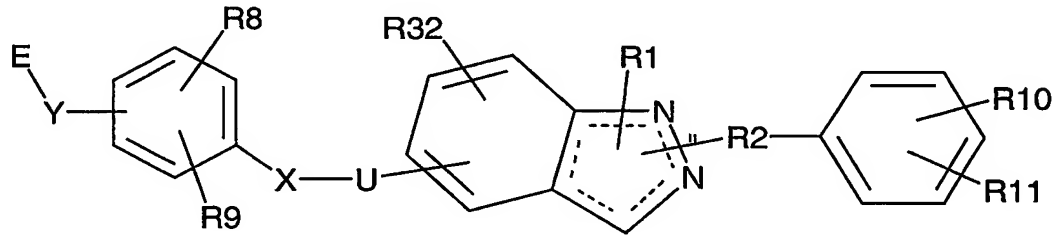
;

wherein n1 is 1 to 5.

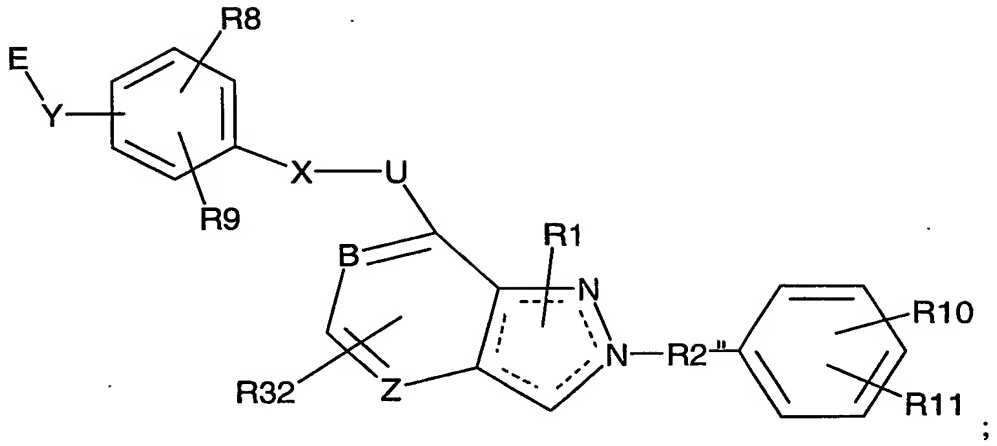
40. A compound as claimed by any one of Claims 1 through 13, 17 through 31, Claims 33 through 36 of the Structural Formula:



41. A compound as claimed by any one of Claims 1 through 13, Claims 17 through 31, Claims 33 through 36 of the Structural Formula:



42. A compound as claimed by any one of Claims 1 through 11, Claims 14 through 28, Claims 30 through 36 of the Structural Formula:



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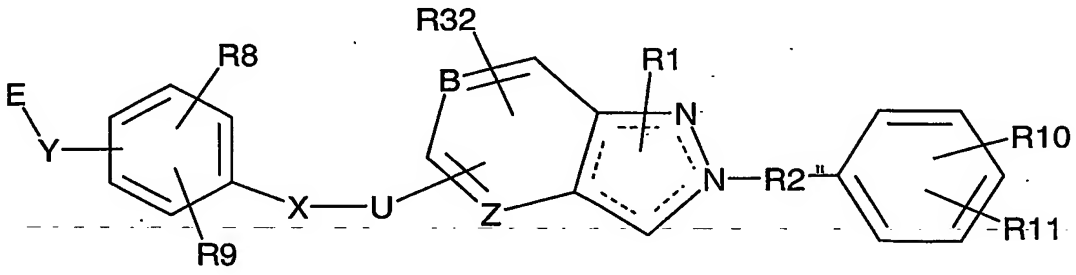
wherein B is N or C; Z is N or C, with the proviso that when Z is C then B is C.

43. A compound as claimed by any one of Claims 1 through 9, Claims 13 through 27, Claims 29 through 42 wherein X is S, Y is selected from the group consisting of C and O, E is CH_2COOH, and R2 is a bond.

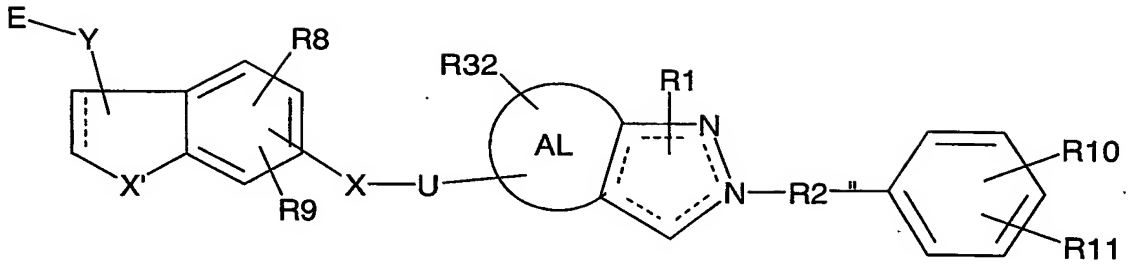
44. A compound as claimed by any one of Claims 1 through 43 wherein R32 is hydrogen, R8 is hydrogen and R9 is C_1-C_4 alkyl.

45. A compound as claimed by any one of Claims 1 through 13, 17, Claims 18 through 32, Claims 34 through 41 of the Structural Formula:



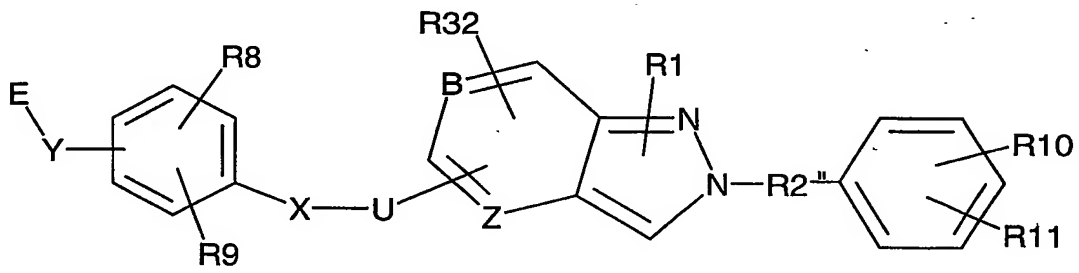
wherein B is N or C; Z is N or C, with the proviso that when Z is C then B is C.

46. A compound as claimed by any one of Claims 1 through 28, Claims 30 through 37 of the Structural Formula:



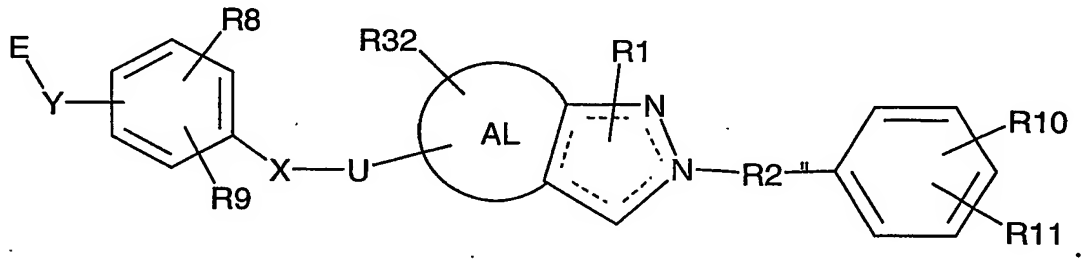
wherein X' is selected from the group consisting of O and S.

47. A compound as claimed by any one of Claims 1 through 13, 16, Claims 18 through 32, Claims 34 through 41 of the Structural Formula X:



wherein B is N or C; Z is N or C, with the proviso that when Z is C then B is C.

48. A compound as claimed by any one of Claims 1 through 13, 16, Claims 18 through 32, Claims 34 through 41 of the Structural Formula: XI:



49. A compound as claimed by any one of Claims 1 through 3 wherein the compound is selected from the group consisting of

2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]phenoxyacetic Acid;

3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]phenyl}propionic Acid;

2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]phenoxyacetic Acid;

3-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]phenylacetic Acid;

6-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]benzo[*b*]thiophen-3-ylacetic Acid;

3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethoxy]phenyl}propionic Acid;

3-{2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethoxy]phenyl}propionic Acid;

(+/-)-2-Methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

(+/-)-2-Methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

(+/-)-3-(2-Methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenyl)propionic Acid;

(+/-)-2-Ethyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

(+/-)-6-{1-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-7yl]ethylsulfanyl}benzo[*b*]thiophen-3-ylacetic Acid;

(+/-)-3-(2-Methyl-4{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7yl]ethoxy}phenyl)propionic Acid;

(+/-)-3-(2-Ethyl-4-{1-[2-(4-trifuoromethylphenyl)-2*H*-indazol-7-yl]ethoxyphenyl)propionic Acid;

2-Methyl-4-{1-methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

2-Methyl-4-{1-methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

3-(2-Methyl-4-{1-methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenyl)propionic Acid;

2-Ethyl-4-{1-methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxyacetic Acid;

6-{1-Methyl-1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}benzo[*b*]thiophen-3-ylacetic Acid;

2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenoxyacetic Acid;

3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenyl}propionic Acid;

2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenoxyacetic Acid;

3-{2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenyl}propionic Acid;

6-[2-(4-Trifluoromethylphenyl)-2H-indazol-6-ylmethylsulfanyl]benzo[*b*]thiophen-3-ylacetic Acid;

3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenyl}propionic Acid;

{6-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]benzo[*b*]thiophen-3-yl}acetic Acid;

2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-ylmethylsulfanyl]phenoxyacetic Acid;

2-Ethyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-ylmethylsulfanyl]phenoxyacetic Acid;

3-{2-Methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-ylmethylsulfanyl]phenyl}propionic Acid;

6-[2-(4-Trifluoromethylphenyl)-2*H*-indazol-4-ylmethylsulfanyl]benzo[*b*]thiophen-3-ylacetic Acid;

2-Methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethylsulfanyl]phenoxyacetic Acid;

2-Ethyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethylsulfanyl]phenoxyacetic Acid;

3-{2-Methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethylsulfanyl]phenyl}propionic Acid;

3-{2-Methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethylsulfanyl]phenyl}propionic Acid;

2-Methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethylsulfanyl]phenoxyacetic Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethoxy]phenoxy}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethoxy]phenylsulfanyl}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-ylmethoxy]phenoxy}propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenylsulfanyl)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenoxy)propionic Acid;

(2-Ethyl-4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)acetic Acid;

(2-Methyl-4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)acetic Acid;

2-Methyl-2-(4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenoxy)propionic Acid;

2-Methyl-2-(2-methyl-4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethoxy}phenoxy)propionic Acid;

2-Methyl-2-(2-methyl-4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)propionic Acid;

2-Methyl-2-(4-{2-[2-(4-trifluoromethylphenyl)-2*H*-indazol-7-yl]ethylsulfanyl}phenoxy)propionic Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenoxy}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenoxy}propionic Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxy]phenylsulfanyl}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-ylmethoxymethyl]phenoxy}propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-6-yl]ethylsulfanyl}phenoxy)propionic Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethoxy]phenoxy}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethoxy]phenylsulfanyl}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-ylmethoxy]phenoxy}propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethoxy}phenylsulfanyl)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-5-yl]ethoxy}phenoxy)propionic Acid;

2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-ylmethylsulfanyl]phenoxy}propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethylphenyl)-2*H*-indazol-4-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[2-(4-trifluoromethyl-phenyl)-2*H*-indazol-4-yl]ethoxy}phenylsulfanyl)propionic Acid;

2-Methyl-2-{2-methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethoxy]phenoxy}propionic Acid;

2-Methyl-2-{2-methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethoxy]phenylsulfanyl}propionic Acid;

2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-ylmethoxy]phenoxy}propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethoxy}phenylsulfanyl)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]ethylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{4,4,4-trifluoro-1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]butoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{4,4,4-trifluoro-1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]butylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{4,4,4-trifluoro-1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]butoxy}phenylsulfanyl)propionic Acid;

(+/-)-2-Methyl-2-(4-{4,4,4-trifluoro-1-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]butoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methoxy}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(2-methyl-4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methoxy}phenylsulfanyl)propionic Acid;

(+/-)-2-Methyl-2-(4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methylsulfanyl}phenoxy)propionic Acid;

(+/-)-2-Methyl-2-(4-{phenyl-[1-(4-trifluoromethylphenyl)-1*H*-indazol-4-yl]methoxy}phenoxy)propionic Acid;

2-Methyl-2-{2-methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethoxy]phenoxy}propionic Acid;

2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethoxy]phenylsulfanyl}propionic Acid;

2-Methyl-2-{2-methyl-4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethylsulfanyl]phenoxy}propionic Acid;

2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethylsulfanyl]phenoxy}propionic Acid; and,

2-Methyl-2-{4-[1-(4-trifluoromethylphenyl)-1*H*-indazol-7-ylmethoxy]phenoxy}propionic Acid.

50. A compound as claimed by any one of Claims 1 through 49 that is in the S conformation.

51. A compound as claimed by any one of Claims 1 through 49 that is in the R conformation.

52. A pharmaceutical composition, comprising as an active ingredient, at least one compound as claimed by any one of Claims 1 through 51 together with a pharmaceutically acceptable carrier or diluent.

53. A method of modulating a peroxisome proliferator activated receptor, comprising the step of contacting the receptor with at least one compound as claimed by any one of Claims 1 through 51.

54. A method of treating diabetes mellitus in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claims 1 through 51.

55. A method of treating Metabolic Syndrome in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claims 1 through 51.

56. A method of selectively modulating a PPAR delta receptor comprising administering a compound as claimed by any one of Claims 1 through 51 to a mammal in need thereof.

57. The manufacture of a medicament for use in the treatment and/or prevention of a condition mediated by nuclear receptors, in particular by a peroxisome proliferator activated receptor, wherein the compound is a compound as claimed by any one of Claims 1 through 51.

58. A method for treating or preventing the progression of cardiovascular disease in a mammal in need thereof comprising administering a therapeutically effective amount of a compound as Claimed by any one of Claims 1 through 51.

59. A method as claimed by Claim 58 wherein the mammal is diagnosed as being in need of such treatment.

60. A method of treating arthritis in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 51.

61. A method of treating demyelating disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 51.

62. A method of treating inflammatory disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 51.

63. A method as claimed by any one of Claims 60, 61, and 62 wherein such mammal is diagnosed as being in need of such treatment.

64. A compound as Claimed by any one of Claims 1 through 51 for use as a pharmaceutical.

65. A compound as claimed by any one of Claims 1 through 51 wherein the compound is radiolabeled.

66. A compound as disclosed by any one of the Examples herein.

67. All methods disclosed herein of preparing the compounds as claimed by any one of Claims 1 through 3.